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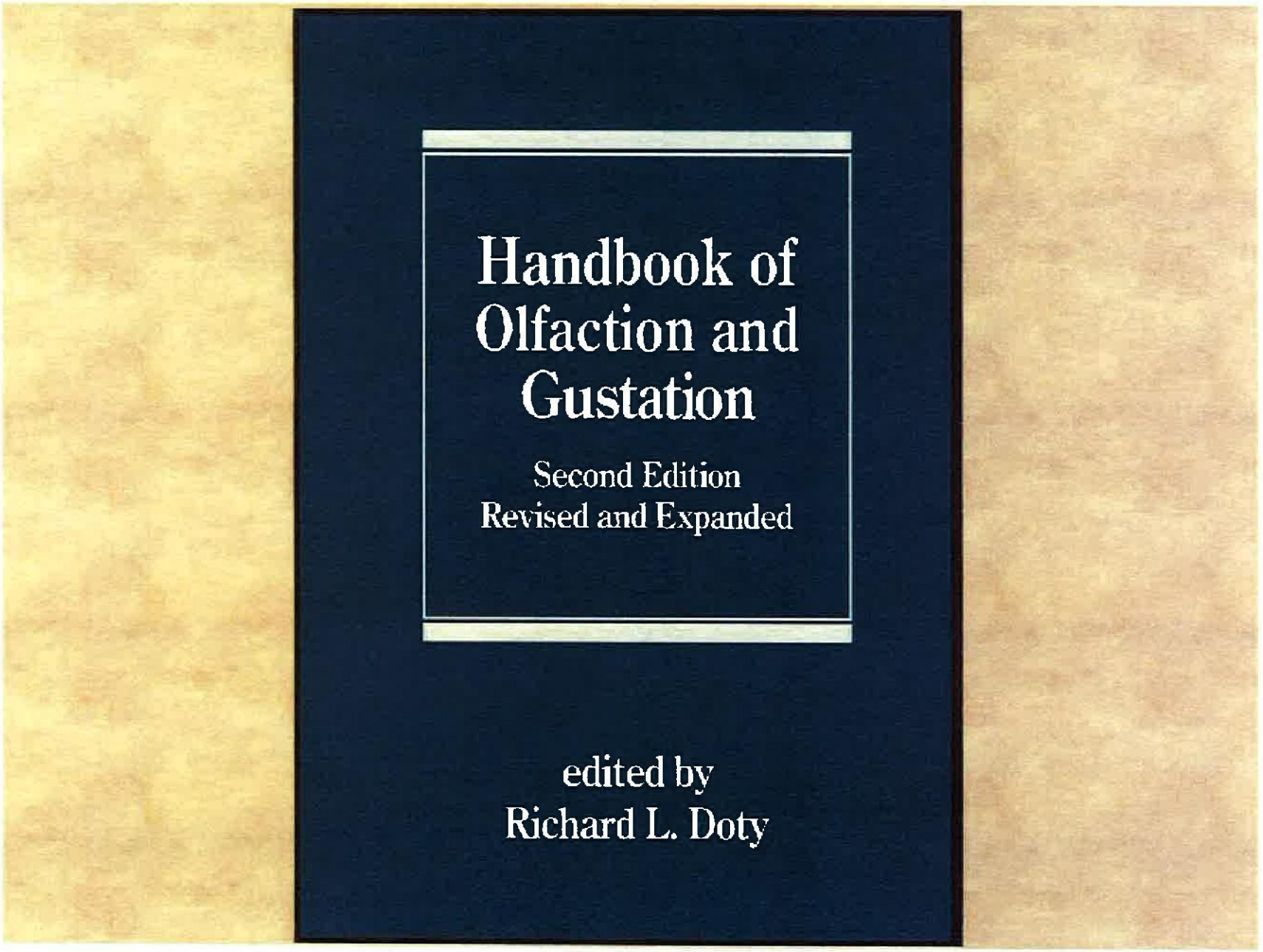
Handbook of
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Psychophysical Measurement of Human Olfactory Function, Including Odorant Mixture Assessment

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I. INTRODUCTION

As can be gleaned from other chapters in this volume, the perception of an odorant depends upon the activation of a subset of ~1000 olfactory receptor types distributed, in the human, across ~6,000,000 receptor cells. Each receptor cell commonly carries only one type of receptor, and the relative distribution of the receptor types among the ~6,000,000 receptor cells is unknown. Since most odorous substances found in nature are comprised of more than one chemical, a typical stimulus simultaneously activates overlapping subsets or arrays of many olfactory receptor cells. From these arrays the nervous system extracts a unitary sensation for a given stimulus, although, for some substances, a few major "notes" can be discerned, as is well known to wine and beer connoisseurs. Hence, from one perspective olfaction is largely a synthetic sensory system, synthesizing a distinct individual sensory sensation from a complex set of chemicals, many of which have an individual odor. From another perspective, however, it is an analytical sensory system, capable of extracting from hundreds of potential sensations a few dominant qualities.

During the last two centuries, numerous tests have been devised to assess the function of this system. Historically, many of these tests have been modeled on procedural and mathematical concepts developed in the mid-nineteenth century by Weber (1834) and Fechner (1860) and by Thurstone, Stevens, and others in the twentieth century (e.g., Anderson, 1970; Stevens, 1961;Thurstone, 1927a, b). Tests derived from these traditions include absolute detection thresholds (the lowest odorant concentration that can be perceived), differential thresholds (the smallest difference in concentration of a given chemical that can be perceived), and various indices of suprathreshold sensation magnitude. Most were developed within the theoretical framework of establishing mathematical rules or laws that govern the build-up of suprathreshold sensation relative to stimulus intensity. To achieve these ends, well-defined stimuli (e.g., single chemicals of known chemical purity) were usually employed, allowing for straightforward stimulus specification.

Other trends, however, resulted in the development or application of tests more useful in applied settings. For example, eighteenth- and nineteenth- century physicians simply presented familiar odorants to patients to see if they could be identified, usually without insight into prior psychophysical developments. In the twentieth century relatively sophisticated procedures were developed within the food industry (e.g., the forced-choice triangle test), where the need exists for quantifying the discriminability or acceptability of various product formulations in relation to perceived qualitative attributes. Unlike the academic psychophysical traditions, and akin to the clinical traditions, the stimuli were multicomponent or chemically complex. Although quantitative, the metrics employed in these paradigms were more operational and rarely linked to simple physicochemical properties such as odorant concentration.

The present chapter has two major goals. The first is to provide the reader with an up-to-date overview of the quantitative methods available for assessing the sense of smell, regardless of the historical traditions that led to their development. Emphasis is placed on the relative utility of various approaches for achieving this end. The second goal is to examine elements of odor mixture perception, including how well individual components can be discerned. An understanding of odor mixture processing is of value in elucidating how the olfactory system works, as its neural architecture seems to be designed to filter or collapse complex arrays of chemical information into distinct, interpretable, and manageable percepts. Although many of the examples described in this chapter come from clinical studies, the tenants of the chapter are broadly applicable to settings outside the clinic, including industrial and regulatory ones.

II. STIMULUS CONTROL AND PRESENTATION

In some chemosensory paradigms, extremely accurate stimulus specification is required, and elaborate olfactometers and other devices for presenting known concentrations of odorants in specific quantities for various durations have been devised (for review, see Prah et al., 1995). This is particularly true for devices employed in event-related potential research (see Chapter 11).

In other paradigms, including those related to assessing olfactory function in patients, it is not necessary to know the exact number of molecules that enter the nose to make the test valid. The key issue in the latter case is that the odorants are presented in a reliable manner and that norms are available to establish whether a patient's responses are normal or abnormal. Thus, accurate clinical assessment of chemosensory function can be made using surprisingly simple stimulus presentation equipment.

Devices used to present odorants to humans include (1) the draw tube olfactometer of Zwaardemaker (1925, 1927), (2) glass sniff bottles (Cheesman and Townsend, 1956; Doty et al., 1986; Nordin et al., 1998), (3) odorized glass rods, wooden sticks, felt-tipped pens, alcohol pads, or strips of blotter paper (Davidson & Murphy, 1997; Hummel et al., 1997; Semb, 1968; Toyota et al., 1978), (4) plastic squeeze bottles (Amoore and Ollman, 1983; Cain et al., 1988; Doty, 2000; Guadagni et al., 1963), (5) air-dilution olfactometers (Cheesman and Kirkby, 1959; Doty et al., 1988b; Kobal and Plattig, 1978; Lorig et al., 1999; Punter, 1983; Walker et al., 1990; Wenzel, 1948), (6) microencapsulated "scratch and sniff" odorized strips (Doty, 1995; Doty et al., 1984a; Richman et al., 1992), and (7)

bottles from which blasts of saturated air are presented (Elsberg and Levy, 1935) (Fig. 1). In environmental control studies, mobile units containing olfactometers, odor exposure chambers, analytical equipment, and subject waiting rooms have been employed (e.g., Berglund et al., 1984; Springer, 1974) (Fig. 2).

In addition to these approaches to the presentation of stimuli, intravenous administration of odorants has been employed to produce chemosensory sensations. This has been used primarily by Japanese otolaryngologists in an attempt to determine whether the olfactory receptors are working when nasal congestion or blockage eliminates or mitigates airflow to the receptor region. The assumption underlying this technique is that the stimulus makes its way to the olfactory receptors via the bloodstream. Most commonly thiamine propyldisulfide (Alinamin) is injected into the median cubital vein, and recordings of the duration and latency of the onset of a garlic-like sensation experienced by the patient are made (see Takagi, 1989, for review). Although this procedure may be of value in some cases, there is some controversy regarding its physiological basis (i.e., whether the stimulus reaches the receptors via diffusion from nasal capillaries, from lung air, or both) (see Maruniak et al., 1983). Furthermore, such testing is invasive, highly variable, not readily adaptable to a forced-choice paradigm, and lacks normative referents.

III. PSYCHOPHYSICAL TEST PROCEDURES

Today, any procedure that provides a quantitative measure of sensory function and requires a verbal or conscious overt response on the part of the examinee is generally considered to be a psychophysical procedure. In this section, the basic psychophysical paradigms available for measuring olfactory function are discussed and examples of their application are provided. The interested reader is referred to other sources for more detailed information about psychophysical methods, including their mathematical foundations (Ekman and Sjöberg, 1965; Gescheider, 1988; Guilford, 1954; Köster, 1975; Marks, 1974; Stevens, 1961; Tanner and Swets, 1954).

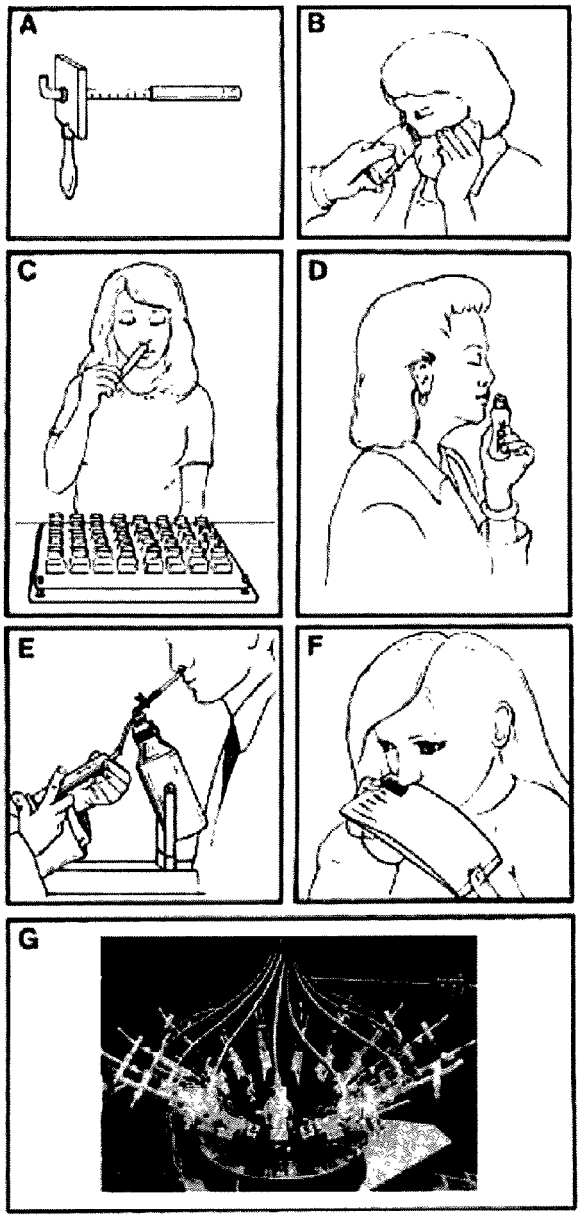

Figure 1 Procedures for presenting odorants to subjects for assessment. (A) Early draw-tube olfactometer of Zwaardemaker. In this apparatus, an

outer tube, made of rubber or another odorous material, slides along a calibrated inner tube, one end of which is inserted into the subject's nostril. When the odorized tube is slid toward the subject, less of its internal surface is exposed to the inspired airstream, resulting in a weaker olfactory sensation. (B) Sniff bottle. (C) Perfumer's strip. (D) Squeeze bottle. (E) Blast injection device. The experimenter injects a given volume of odor into the bottle and releases the pressure by squeezing a clamp on the tube leading to the nostril, producing a stimulus pulse. (F) Microencapsulated "scratch-and-sniff" test. (G) Sniff ports on a rotating table connected to one of the University of Pennsylvania's dynamic air-dilution olfactometers.

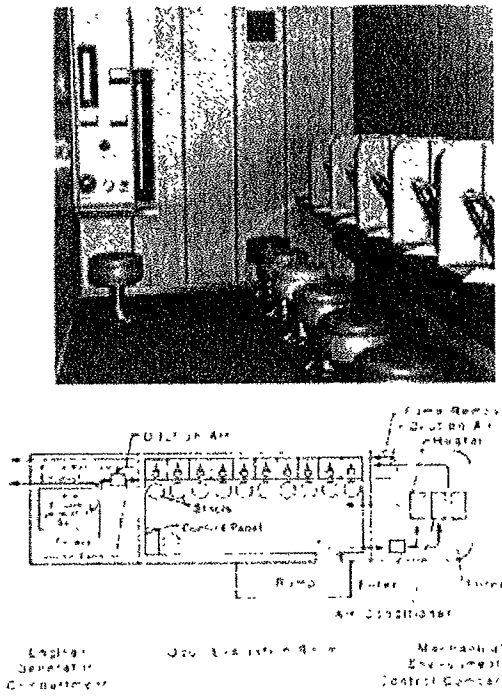

Figure 2 (Top) Odor evaluation room of mobile odor evaluation laboratory designed to evaluate responses of panel members to diesel exhaust. (Bottom) Schematic of mobile odor evaluation laboratory. (From Springer, 1974.)

A. Detection and Recognition Threshold Tests

A popular means for assessing chemosensory function is to establish, operationally, a measure of the lowest concentration of a stimulus that can be detected. A qualitative odor sensation (e.g., "banana-like") is rarely perceived at very low odorant concentrations, where only the faint presence of something is noted. The absolute or detection threshold is the lowest odorant concentration where such a presence is reliably detected, whereas the recognition threshold is the lowest concentration where odor quality is reliably discerned. In modern olfactory detection threshold testing, a subject is asked to indicate, on a given trial, which of two or more stimuli (e.g., a low concentration odorant and one or more nonodorous blanks) smells strongest, rather than to report whether an odor is perceived or not. Recognition thresholds are obtained in a similar manner, but the

requirement is to report which one has the target quality. Such "forced-choice" procedures are less susceptible than non-forced-choice procedures to contamination by response biases (i.e., the conservatism or liberalism in reporting the presence of an odor under uncertain conditions). In addition, they are typically more reliable and produce lower threshold values (Blackwell, 1953; Doty et al., 1995).

Two types of threshold procedures that have received the most clinical use are the ascending method of limits (AML) and the single staircase (SS) procedures. In the AML procedure, odorants are presented sequentially from low to high concentrations and the point of transition between detection and no detection is estimated. Forcedchoice responses are required on each trial. In the SS method (a variant of the method of limits technique) (see Cornsweet, 1962), the concentration of the stimulus is increased following trials in which a subject fails to detect the stimulus and decreased following trials where correct detection occurs. In both these procedures, the direction of initial stimulus presentation is made from weak to strong in an effort to reduce adaptation effects of prior stimulation (see Pangborn et al., 1964).

An example of a clinical application of the AML procedure is provided by Cain (1982a) who used 60-mL glass sniff bottles to present either water (diluent) or odorant (n-butanol dissolved in water) to 43 patients with various degrees of olfactory dysfunction. Four repeated ascending series were presented to each side of the nose in a twoalternative, forced-choice format. This test, which took approximately half an hour per patient to administer, demonstrated that the olfactory dysfunction in these cases was typically bilateral.

An example of the clinical use of a SS procedure comes from a study that demonstrates loss of olfactory function in early Alzheimer's disease (Doty et al, 1987). In this experiment, a trial consisted of the presentation of two 100-mL glass sniff bottles to the patient in rapid succession. One bottle contained 20 mL of a given concentration of phenyl ethyl alcohol dissolved in USP-grade light mineral oil, whereas the other contained mineral oil alone. The patient was asked to report which of the two bottles in a pair produced the strongest sensation. The first trial was presented at a -6.50 log (liquid volume/volume) concentration step. If a miss occurred on any trial before five were correctly completed at that concentration, the process was repeated at 1 log concentration step higher. When five consecutive correct trials occurred at a given concentration level, the staircase was "reversed" and the next pair of trials was presented at a 0.5 log concentration step lower. From this point on, only one or two trials were presented at each step (i.e., if the first trial was missed, the second was not given and the staircase was moved to the next higher 0.5 log step concentration). When correct performance occurred on both trials, the concentration of the next trial was given at 0.5 log unit step lower. The average of the last four of seven staircase reversal points served as the threshold estimate. Examples of individual data obtained using the SS procedure are shown in Figure 3.

In general, threshold values are relative and dependent upon such factors as the method of stimulus dilution, volume of inhalation, species of molecule, type of psychophysical task, and number of trials presented (Pierce et al, 1996). A number of investigators have been struck with the fact that threshold measures often exhibit considerable intra- and intersubject variability. For example, in one study of 60 subjects, intersubject variation as great as 5 log units was reported (Brown et al., 1968). In another, in which a nonforced-choice ascending threshold procedure was used (the Japanese

"T&T Olfactometer"), variation on the order of 16 log units was present among groups of 430–1000 young subjects (Yoshida, 1984). More recently, Stevens et al. (1988) obtained 60 threshold values over the course of 30 days from three subjects (20 for butanol, 20 for pyridine, and 20 for β-phenylethylmethylethylcarbinol). These investigators found that the within-subject variability across test days was as great as the between-subject variability on a given test day, suggesting to these authors that the large individual differences observed in threshold values are not a reflection of big differences among stable threshold values of subjects but reflect large day-to-day fluctuations in the test measures. Unfortunately, much of this fluctuation likely reflects the use of the single ascending detection threshold technique, in which the apparent limen is traversed only once. Clearly, test procedures with more trials, such as the SS procedure, produce less variable measures and, when employed, do not exhibit as marked day-to-day fluctuations.

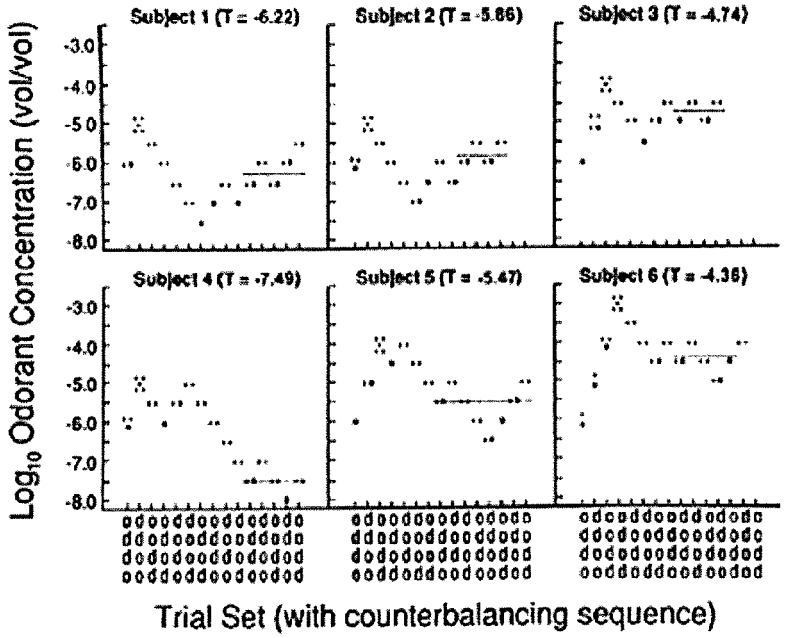

Figure 3 Data illustrating single-staircase detection threshold determinations. Each plus (+) indicates a correct detection when an odorant versus a blank is presented. Each zero (0) indicates an incorrect report of an odorant. Threshold value (T; vol/vol in light USP grade mineral oil) is calculated as the mean of the last four

of seven staircase reversals. Although the geometric mean is the correct measure, the arithmetic mean usually provides a close approximation. The o's and d's on the abcissa indicate the counterbalancing order of the presentation sequences for each trial and are read downward (o-odorant presented first, then diluent; d-diluent presented first, then odorant). In the first reversal point (where five correct sets of pairs occur at the same concentration), the fifth order sequence is determined by the first o or d of the subsequent column of four order sequences. (From Doty, 1991a.)

B. Difference Threshold Tests

In classical psychophysics, the smallest amount by which a stimulus must be changed to make it perceptibly stronger or weaker is termed a "just noticeable difference," or JND. This value is also called a difference or differential threshold (in contrast to an absolute threshold, as described above). The size of the increment in odorant concentration (ΔI) required to produce a JND increases as the comparison concentration (I) increases, with the ratio approximating a constant; i.e., $\Delta I/I=K$ (Weber's law) (Weber, 1834). K is a rough index of the sensory system's sensitivity (i.e., the smaller the K value, the more sensitive the system is to fine changes in stimulation). However, numerous studies suggest that K is not a constant, being influenced by the size of I, particularly at the extremes of the sensory continuum (Doty, 1991a).

An example of a brief clinical test used to establish a difference threshold is described by Eichenbaum et al. (1983). In this test, 10 binary dilutions (in water) of acetone, ethanol, almond extract, and lemon extract were presented. Initially, the highest and lowest concentrations of a given odorant were presented and the subject was required to choose the stronger stimulus. Successively stronger stimuli were then paired with the strongest stimulus until, on the last of the 10 trials, the two samples were identical. Eichenbaum operationally defined the difference threshold as the lowest concentration for which discrimination up to and including the dilution was effortless.

C. Signal Detection Tests

Signal detection theory (SDT) differs fundamentally from the approach of sensory measurement inherent in classical threshold theory. Thus, SDT rejects the notion of a threshold (whether absolute or differential) and focuses on (1) noise and signal plus noise

as the milieu of the detection situation and (2) the influences of subject expectancies and rewards on the detection decision. Signal detection procedures provide both a measure of sensory sensitivity and the subject's response criterion or bias (Tanner and Swets, 1954). In effect, the response criterion is the internal rule used by a subject in deciding whether or not to report detecting a stimulus (e.g., the liberalism or conservatism in reporting a sensation under uncertain circumstances). For example, two subjects may experience the same subtle degree of sensation from a very weak stimulus. One, however, may report that no sensation was perceived (e.g., perhaps because of lack of self-confidence), whereas the other may report the presence of the sensation. In both cases, the stimulus was perceived to the same degree. However, the two subjects had different criteria for reporting its presence. In

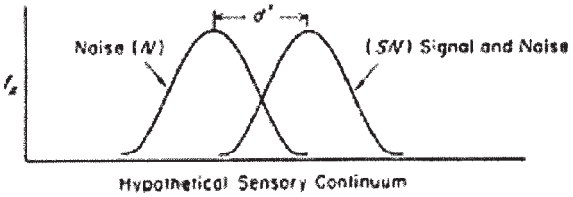

Figure 4 Hypothetical distributions of signal plus noise (SN) and noise alone (N) plotted on the same axes. When the strength of the perceived signal increases, the SN distribution moves to the right, increasing d, the measure of the distance between the two distributions in standard deviation units (z-scores). (From Doty, 1976.)

a traditional non-forced-choice detection threshold paradigm, the investigator would conclude that these two subjects differed in sensitivity to the stimulus, when, in fact, they only differed in regards to their response biases.

SDT assumes that a stimulus is imbedded within a background of noise. Noise can arise from a variety of sources and can be conceptualized at a number of levels (e.g., variations in attention, stimulus fidelity, neural firing unrelated to the stimulus, fluctuations in distracting physiological processes). In most cases noise is assumed to be normally distributed (as is done here to simplify discussion). Whenever a signal is added to the "noise" (N) distribution, a "signal plus noise" (SN) distribution results. Both the N and SN distributions can be placed on the same set of axes, as shown in Figure 4. The measure of the subject's sensitivity is the distance between the means of these distributions.

The concept of the response criterion is illustrated for a hypothetical subject in Figure 5 (Doty, 1991a). On any given trial, a low-concentration odorant (SN) or a blank stimulus (N) is presented, and the subject's task is to report whether or not an odor was presented.

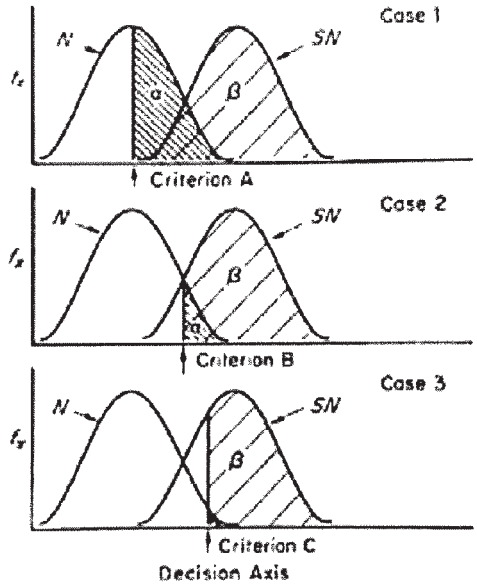

Figure 5 Hypothetical examples of how the response criterion can vary when perceptual sensitivity (d′) remains constant. In case 1, a liberal criterion was chosen in which a relatively large number of false positives occurred [i.e., a, the reports of the presence of odor when the blank (N) is presented]. In cases 2 and 3 more conservative criteria were chosen, decreasing both the number of false positives (α) and hits (β). Traditional threshold measures confound the influences of perceptual sensitivity and the setting of the response criterion. (From Doty, 1976. Copyright © 1976, Academic Press.)

Reports of "yes" are represented by the areas under the N and SN curves to the right of the vertical line depicting the subject's response criterion, whereas reports of "no" are indicated by the areas to the left of this line. In case 1, the subject exhibits a very liberal criterion, reporting the presence of an odor on the majority of the SN trials ((3) and on half of the N trials (a). Thus, although correct detection of the odorant occurred nearly all

of the time (β), many false alarms (a) were present. Perhaps in this instance the subject was rewarded for reporting the detection of an odor and not admonished for making false alarms. In case 2, the subject chose a less liberal response criterion. Although fewer correct detections of the odor were made (β), fewer false alarms were also made (a). In case 3, the observer chose a very conservative response criterion, making few false alarms but similarly making fewer correct detections. This would tend to result, for example, when a subject is penalized for making false positives and given few rewards for successful detection of the odor. In all three of these hypothetical cases, the sensitivity (i.e., d′) was equivalent, as indicated by the constant distance between the N and SN distributions.

In a typical olfactory experiment employing SDT, the subject is presented with a large number of trials of a single low concentration of odorant interspersed with blank trials (Doty et al, 1981; Semb, 1968). Even though the number of blank and odorant trials need not be equivalent, this is commonly the case. The proportion or percent of the total odor trials (S) on which a subject reports detecting an odor (the hit rate) is calculated, as is the percent of blank trials (N) on which an odor is reported (the false alarm rate). The parametric sensitivity measure, d′, can then be computed by converting the proportions to normal distribution standard deviation values (z-scores) via a normal probability table; d′ equals the z-score for hits minus the z-score for false alarms. A more convenient procedure for determining d′ for any combination of hit and false-alarm proportions is to use the table provided by Elliot (1964). In addition, nonparametric signal detection measures are also available (Brown, 1974; Frey and Colliver, 1973; Grier, 1971; Hodos, 1970; but see Macmillan and Creelman, 1996), as are methods for testing the parametric assumptions of traditional signal detection analysis (Gescheider, 1976; Green and Swets, 1966).

The classical parametric measure of response bias is termed β. Not to be confused with the β in Figure 5, β represents the ratio, at the criterion point, of the ordinate of the SN distribution to that of the N distribution. This value can be easily calculated from the hit and false-alarm rates by use of ordinate values from the normal curve, as discussed by Gescheider (1976).

Despite the fact that hundreds of trials have traditionally been used in signal detection studies, some chemical senses studies have employed far fewer trials, largely out of practicality considerations. For example, Potter and Butters (1980) and Eichenbaum et al. (1983) computed d′ using only 30 test trials. Even though such estimates are somewhat unstable (because a test's reliability is a function of its length), they may be less so than typically assumed, and there is at least some empirical rationale for the use of abbreviated signal detection tests. Thus, O'Mahony et al. (1979b), in a study of gustatory sensitivity to sodium chloride, found that Brown's (1974) nonparametric R index fell, after 40 trials, within 5% of the values obtained after 200 trials in slightly over half the subjects tested. However, an analogous olfactory study has not been performed, and ideally all of the subjects should evidence such response stability. For these reasons it is prudent to use as many trials as possible in signal detection tasks.

D. Suprathreshold Scaling Procedures

A number of psychological attributes can be assigned to odors, including strength, pleasantness, and quality. Although the first of these attributes changes in a systematic way with stimulus concentration, odorant pleasantness or unpleasantness is more variable and idiosyncratic (see Doty, 1975). In regard to odor quality, only in rare instances is it dramatically altered by changes in suprathreshold odorant concentration. Since the perceived intensity of an odorant is a function of its concentration, ratings or other measures of perceived intensity have been used to evaluate olfactory function. Because the intensity of a stimulus is related to the number of neurons that are recruited and the frequency at which they fire, such measures may relate to the extent of neural damage present in the afferent pathway (Drake et al., 1969). However, suprathreshold rating or scaling methods appear to be less sensitive to olfactory dysfunction than a number of other tests (e.g., detection threshold tests and tests of odor identification), although they have the advantage of being relatively brief, easy to administer, and less susceptible than threshold tests to subtle stimulus contamination. Negative findings, however, must be conservatively interpreted, as in some cases suprathreshold rating scales have completely missed major changes observed by other methods (e.g., the influences of age on olfactory function) (see Rovee et al., 1975).

Despite the fact that olfactory psychophysicists and psychometricians have sought to develop psychological scales with ruler-like properties (i.e., the so-called ratio scale, where distances along the scale have ratio properties and a true zero point is present), the degree to which this is possible is debatable. Judgments of the intensity of odors must be viewed as relative, as they are markedly influenced by both subject idiosynerasies and contextual factors (e.g., a moderately intense odor is reported to be more intense when presented with weak comparison stimuli than with strong comparison stimuli) (Eyman et al., 1975; Helson, 1964). Fortunately, for the purposes of clinical testing, neither the exact form of the underlying psychological scale nor the influences of stimulus context need to be of great concern to the examiner, as long as the test procedures are standardized and it can be demonstrated that the responses on the scaling tasks are reliable and differentiate among persons with differing degrees of olfactory function.

Rating scales can be used to estimate the relative amount of a psychological attribute perceived by a subject. In chemosensory assessment, two types are popular: category scales, where the relative amount of a sensation is signified by indicating which of a series of discrete categories best describes the sensation, and line scales (also termed visual analog or graphic scales), where the subject or patient indicates the strength of the sensation by placing a mark along a line that has descriptors (termed anchors) located at its extremes (e.g., very weak–very strong). Recently, scales have been developed in which logarithmic elements have been incorporated into their design in an effort to overcome ceiling effects and to more closely mimic ratio-like properties of magnitude estimation (see below) (e.g., Green et al., 1996; Neely et al., 1992). The reader is referred elsewhere to discussions of the properties of rating scales, including the influence of category number on their psychometric properties (Anderson, 1970; Doty, 1991b; Guilford, 1954).

Intensity matching procedures have also been applied in the clinical and other applied settings, with cross-modal matching procedures (e.g., magnitude estimation) being the most popular. In cross-modal matching, the relative magnitude of each member of a stimulus set is estimated by using some other sensory modality or cognitive domain. A

key difference between this procedure and rating scale procedures is that the ratio relations among the intensities of the different stimuli are defined, and the subject's responses are not confined to categories or a short response line. Continua commonly used in the cross-modal matching task termed magnitude estimation include number (e.g., assigning numbers proportionate to an odor's intensity) and distance (e.g., pulling a tape measure a distance proportional to an odor's intensity) (Berglund et al., 1971; Stevens, 1961). When intensities of sensations from two or more modalities are judged on a single common scale, the procedure is termed the method of magnitude matching. Magnitude estimation and magnitude matching are among the most commonly used cross-modal matching procedures and are discussed in more detail below.

In the typical magnitude estimation paradigm, the subject assigns numbers relative to the magnitude of the sensations. For example, if the number 60 is used to indicate the intensity of one concentration of an odorant, a concentration that smells four times as intense would be assigned the number 240. If another concentration is perceived to be half as strong as the initial stimulus, it would be assigned the value 30. The examinee can assign any range of numbers to the stimuli, as long as they reflect the relative magnitudes of the perceived intensities. In some cases, a standard for which a number has been preassigned (often the middle stimulus of the series) is presented to the subject in an effort to make his or her responses more reliable. In other cases, the individual is free to choose any number system he or she wishes, as long as the numbers are made proportional to the magnitude of the attribute (the "free modulus method"). For example, one subject may choose to assign the first stimulus the number 250, whereas another may choose to assign this same stimulus the number 5. If a second stimulus is perceived to be 10 times stronger than the first by each of these individuals, the first one would assign the number 2500, whereas the second one would assign the number 50. The important point is that the absolute values of the numbers are not important; only the ratios between them are relevant.

To obtain an index of suprathreshold function, magnitude estimation data are most commonly plotted on log-log coordinates (log magnitude estimates on the ordinate and log odorant concentrations on the abscissa) and the best line of fit determined using linear regression. The resulting function, $\log P = n \log \Phi + \log k$, where P=perceived intensity, k=the Y intercept, Φ=stimulus concentration, and n=the slope, can be represented in its exponential form as a power function, $P = k\Phi^n$, where the exponent n is the slope of the function on the log-log plot. In olfaction,

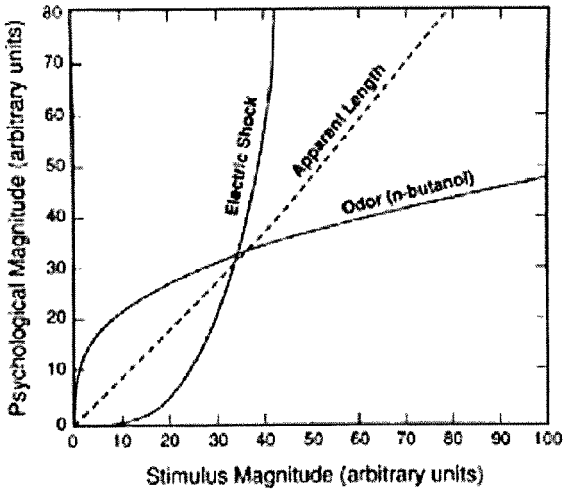

Figure 6 Relationship between perceived magnitude of three types of stimuli, as measured by magnitude estimation, and stimulus magnitude. Note that the perceived intensity of the example odorant increases in a negatively accelerated fashion, indicating a power function exponent less than 1 (in this case 0.33). (Adapted and modified from Stevens, 1961.)

n varies in magnitude from odor to odor, but is generally less than 1, reflecting a negatively accelerated function on linear-linear coordinates (Fig. 6). As noted elsewhere, various investigators have made modifications in these equations in an attempt to take into account such factors as threshold sensitivity and adaptation (Doty, 1991a; Overbosch, 1986).

It is noteworthy that magnitude estimation, perhaps more so than most other sensory procedures, can be biased or influenced in systematic ways by procedural and subject factors (Doty, 1991a; Marks, 1974). The magnitude estimation task is relatively complex in that accurate responses to a stimulus require a good memory for the prior stimulus. If too much time lapses between the presentation of stimuli, the memory of the prior stimulus fades. On the other hand, if the trials are spaced too closely together, adaptation can distort the relationship. Not all subjects consistently provide ratio estimates of stimuli, and a number do not understand the concept of producing ratios (Baird et al, 1970; Moskowitz, 1977). Furthermore, the magnitude of the exponent is dependent on

the choice of the stimulus scale (i.e., the units in which the stimulus concentration is expressed), although in olfaction this is probably of minor consequence (Myers, 1982).

The degree to which these and other potential shortcomings hinder the use of magnitude estimation procedures in applied settings, such as the clinic, is not known; however, it is likely that such problems can be minimized by ensuring that the instructions, test procedures, and test stimuli are carefully standardized and monitored. Comparative assessments of nine-point rating scales, line scales, magnitude estimation scales, and a hybrid of category and line scales suggest that, for untrained or mathematically unsophisticated subjects, category scales and line scales may be superior to magnitude estimation when such factors as variability, reliability, and ease of use are considered (Lawless and Malone, 1986a,b).

Since the magnitude estimation function's intercept and height above the origin depend to a large degree on idiosyncratic differences in the use of numbers and the specific magnitude estimation method employed (e.g., fixed vs. free modulus), only its slope has traditionally been used as an index of sensory function. In an attempt to gain additional information from the function's ordinate position, investigators have employed the method of cross-modal magnitude matching, which provides, at least theoretically, information about the perceived intensity of stimuli from the absolute position of the magnitude estimation function and corrects, to some degree, for differences among subjects in number usage (for a detailed discussion of this procedure, see Marks et al., 1988). In the most common application of this method, judgments of the intensity of sensations from two modalities (e.g., loudness and odor intensity) are made on a common magnitude estimation scale (Marks et al., 1986). Under the assumption that subjects experience stimuli on one of the continua (i.e., loudness) in a similar manner (an assumption that some question), differences among their loudness ratings would be expected to reflect differences in number usage. The odor intensity continuum can then be adjusted accordingly. Such normalization allows, theoretically, for a direct comparison of scale values across subjects; thus, if the adjusted odor intensity magnitude value for one subject is 10 and for another subject is 20 at the same concentration level, the second subject is presumed to experience twice the odor intensity as the first subject.

E. Quality Discrimination Tests

The most straightforward chemosensory quality discrimination test requires individuals to decide whether two stimuli have the same or different quality. In one scenerio, a series of same-odorant and different-odorant pairs is presented, and the proportion of pairs that are correctly differentiated is taken as the measure of discrimination (O'Mahony, 1979; O'Mahony et al, 1979; Potter and Butters, 1980;). Variants on this theme include picking the "odd" stimulus from a set from which only the "odd" stimulus differs (e.g., the socalled triangle test) (Frijters et al, 1980).

Another form of discrimination test is based on a procedure called multidimensional scaling (MDS). In one variant of this procedure, ratings are made for all possible pairs of stimuli (or selected subsets of pairs) on a line scale anchored with descriptors like "completely different vs. exactly the same," and the correlation matrix among these ratings is subjected to an algorithm that places the stimuli in two- or more dimensional space relative to their perceived similarities (e.g., Schiffman et al., 1981). The process is

akin to constructing a map of a country from a list of distances available between the cities of that country. Persons with poor discrimination abilities fail to discern differences and similarities among stimuli, as illustrated by multidimensional spaces that have no distinct or reliable groupings. Because of its time-consuming nature and the fact that statistical procedures for comparing one person's MDS space to another's (or to a norm) are poorly worked out, MDS has not been used routinely in the clinic. Interestingly, when subjects are asked to rate the similarity of stimuli that are only indicated to them by name (i.e., the odorants, per se, are never presented), stimulus spaces derived by MDS are analogous to those obtained by the actual use of the odorants (Carrasco and Ridout, 1993; Ueno, 1992). This implies that well-defined imagery, or at least conceptual representations, exist for odorous stimuli.

Recently, Wise and Cain (2000) used a response latency approach to determine the discriminability of unmixed odors and mixed odors. A clear monotonic relationship was found between latency and accuracy, with latency decreasing with accuracy. In addition, subjects required more time and made more errors in discriminations between binary mixtures and their unmixed components than between the unmixed components. It was concluded that this approach may provide a novel measure of differences in odor quality, since latency provides information about discriminability.

F. Quality Recognition Tests

Two general classes of quality recognition tests can be defined. In the first class, the subject is asked whether each stimulus of a presented set is recognized. Identification is not required. As indicated at the beginning of the chapter, this procedure is relatively crude, despite the fact that it is perhaps the most common means used by neurologists to measure olfactory function (Sumner, 1962). In the second class, a patient is presented with a "target" stimulus and subsequently asked to select the target from a larger set of stimuli. The number of correct responses of a series serves as the test score.

A variant on this theme is the stimulus matching task, in which a set of stimuli are provided and the subject is required to match the stimuli, one by one, to those of a set of identical stimuli. As an example, Abraham and Matha (1983) presented subjects with eight vials that contained four odorants (two vials per odor). The subject's task was to pair up the equivalent two-vial containers. The number of pairs correctly matched on each of two administrations of the test was used by these authors as the test score.

G. Quality Identification Tests

Among the most popular procedures for assessing taste and smell function are those that require stimulus quality identification. Such tests can be divided into three groups: naming tests, yes/no identification tests, and multiplechoice identification tests. The respective responses required, on a given trial, in these three classes of tests are (1) to provide a name for the stimulus, (2) to signify whether the stimulus smells like an object named by the examiner (e.g., does this smell like a rose?), and (3) to identify the stimulus from a list of names or pictures.

Odor naming tests in which no response alternatives are provided have been used clinically (e.g., Gregson et al., 1981) but are of limited value since many normal

individuals have difficulty in naming or identifying even familiar odors without cues. Yes/no identification tests are much more useful, since they require a patient to report whether or not each of a set of stimuli smells like a particular substance named by the experimenter. Two trials with each stimulus are usually given, with the correct alternative provided on one trial and an incorrect one on the other (e.g., orange odor is presented and the subject is asked on one trial whether the odor smells like orange and on another trial whether the odor smells like peppermint). Although such a test requires the patient to keep the percept in memory long enough to compare it with the target word (which, of course, must also be recalled from memory), some of its proponents argue that it is less influenced by cognitive and memory demands than multiple-choice identification tests (see below). Since chance performance on this type of test is 50% compared to 25% on a four-alternative multiplechoice identification test, its range of discriminability is lower, and therefore more trials are needed to obtain the same statistical power as the multiple-choice odor identification test.

Numerous multiple-choice odor identification tests have been described in the clinical literature (Cain et al., 1983; Doty, 1991b; Doty et al., 1984a; Gregson et al., 1981; Wood and Harkins, 1987; Hummel et al., 1997; Wright, 1987). These tests are conceptually similar and, in the few cases that have been examined, strongly correlated with one another (Cain and Rabin, 1989; Doty et al., 1994; Wright, 1987). The most widely used of these tests [the University of Pennsylvania Smell Identification Test (UPSIT), commercially termed the Smell Identification Test™, Sensonics, Inc., Haddon Heights, NJ] examines the ability of subjects to identify, from sets of four descriptors, each of 40 "scratch and sniff" odorants (Fig. 1) (Doty, 1995; Doty et al., 1984a,b). The number of correct items out of 40 serves as the test measure; this value is compared to norms and a percentile rank is determined, depending on the age and gender of the subject (Fig. 1F) (Doty, 1995). This test has several unique features, including amenability to self-administration and a means for detecting malingering (see Sec. VI). Furthermore, it is available in English, French, German, and Spanish versions. The popularity of this test is attested to by the fact that hundreds of scientific publications have arisen from its use by investigators from many laboratories and clinics.

Several odor identification confusion matrix tests have been described that are applicable to clinical settings (Köster, 1975; Wright, 1987). The test that has been most widely applied is that of Wright's (1987). In his test, each of 10 suprathreshold stimuli is presented to a patient in counterbalanced order 10 times (100 total trials). The response alternatives are the names of the 10 stimuli: ammonia, chlorine bleach, licorice, mothballs, peppermint, roses, turpentine, vanilla, Vicks vapor rub, and vinegar. No feedback as to the correctness of the subjects' responses is given. The percentage of responses given to each alternative for each odorant is determined and displayed in a rectangular matrix (stimuli making up rows and response alternatives making up equivalently ordered columns). Responses along the negative diagonal therefore represent correct responses, whereas those that fall away from the diagonal represent "confusions." The percentage of correct responses is used as the main test measure, although some of its proponents argue that the confusions (off-diagonal responses) may provide meaningful clinical information.

The main limitations of Wright's confusion matrix are (1) its long administration time (approximately 45 min) and (2) the lack of evidence that the off-diagonal responses

provide any meaningful clinical information (although such responses may be of value in detecting malingering) (see Kurtz et al., 1999). It would seem that if off-diagonal responses are to be sensitive to aberrations or distortions seen in most clinical cases, more subtle differences in the response alternatives need to be employed within the matrix. Should subtle aberrations be reliably categorized, this approach would have considerable clinical value.

H. Memory Tests

In a basic odor recognition memory test, a subject is required to smell an odorant or a small set of odorants (termed the target or inspection stimulus or stimulus set) and to select, after an interval of time (e.g., 30 sec up to several days), that odorant or set of odorants from foils (distracters). Repeated trials may be performed at one or more retention intervals for each of several stimuli or sets of stimuli. In an effort to minimize the rehearsal of verbal labels reflecting the odor qualities or referents during the delay intervals, the examinee is sometimes asked to perform an unrelated task during the retention period, such as counting backwards by twos or threes. The proportion of trials where correct performance occurs is a typical measure derived from such tests.

The results from an odor memory test must be interpreted with caution. Despite attempts to minimize labeling of the inspection odor with a familiar word or item on the part of a subject, such labeling undoubtedly occurs, and, thus, what is being measured across intervals is the memory of the label, not the memory of the odor. In other words, once an individual recognizes an odor as that of an orange, all that has to be remembered over time is the concept "orange," not the specific smell of the orange. Later, when given stimuli from which to select the earlier perceived odor, the subject simply looks for the smell of an orange (which has been known for much of his or her life). In effect, the odor is not what is being uniquely remembered over the retention interval, only its name or concept. For this reason, investigators have attempted to employ novel, nondescript, and unfamiliar odorants in such tasks. Unfortunately, it is difficult to find target odors and foils that are not readily labeled by subjects as pleasant or unpleasant, fruity or nonfruity, medicine-like or non-medicine-like, etc. In general, both short- and long-term odor recognition is markedly facilitated by verbal encoding (Jehl et al., 1997).

Another point that should be stressed about odor memory tests is that the performance across the delay intervals comprises the "memory" component of the task, not the overall test score. Thus, an odor memory test is essentially an odor discrimination test with varying inspection (delay) intervals. If, for example, scores on a nominal odor memory task differ between two groups (as evidenced by a main group effect in an analysis of variance), then a significant interaction term between delay interval and group must be present for such scores to reflect differences in odor memory per se. Without an interaction with delay interval, the difference would reflect discrimination, not memory. That being said, a number of examples of clinical applications of odor memory tests are available from the literature. Unfortunately, convincing evidence for a true odor memory deficit is lacking in most cases.

Campbell and Gregson (1972) developed a test of shortterm odor memory in which four odors in a row were presented and the patient was asked if the fourth, which was the same as one of the first three, was equivalent to the first, second, or third odorant. No

delay interval, per se, was defined between the presentation of the stimuli, but presumably the trials were presented closely after one another. Seven three-odor combinations of 12 inspection stimuli were administered. Patients who had difficulty with this task were subsequently given two-odor combinations. The test score was the number of odors that were consistently recognized by the subject. This test was shown to be sensitive to olfactory deficits due to schizophrenia (Campbell and Gregson, 1972), Kallmann's syndrome (Gregson and Smith, 1981), and Korsakoff psychosis (Gregson et al., 1981). However, it is debatable whether the scores truly reflect memory processes per se.

Jones et al. (1975) presented 20 pairs of odorants at 0- and 30-second delay intervals to 14 alcoholic Korsakoff psychosis patients, 14 alcoholic controls, and 14 nonalcoholic controls. On a given trial, the subject's task was to report whether the second stimulus was the same as or different from the first. In the 30-second delay interval, the subjects counted backward by threes. Since the Korsakoff psychosis patients performed significantly more poorly than did the control groups at *both* the 0- and 30-second retention intervals, it is questionable whether odor memory is the trait being influenced in this case.

More recently, Jones-Gotman and Zatorre (1993) reported that, in patients having undergone surgical cerebral extirpation for control of epilepsy, odor memory impairment was noted between the controls and two of the eight surgical groups evaluated—namely, those who had received excision from the right temporal or right orbitofrontal cortices. The memory task consisted of eight target odors and eight new foils, and the yesno recognition testing was performed twice after the initial testing—20 minutes later and 24 hours later. Although the authors interpret their findings as evidence of a "right hemisphere predominance in odor memory," their underlying data do not support the notion that differences in odor memory, per se, were present among the groups. Thus, in the overall analysis, where the test scores at the various delay intervals were evaluated as a function of operative group and delay interval, main effects of both of these factors were noted, but no interaction between them was present. No interactions with delay interval were noted in any subgroup analyses. Hence, this study suggests that odor discrimination is altered by certain cerebral excisions, but not necessarily odor memory.

IV. TEST RELIABILITY

The utility of an olfactory test reflects the degree to which it is reliable (consistent, dependable, or stable) and valid (accurately measures what it portends to measure). Related to a test's validity are its sensitivity (ability to detect abnormalities when present) and specificity (ability to detect abnormalities with a minimum number of false positives). Although a test cannot be valid without being reliable, the reverse is not the case; i.e., a test can be reliable but not valid. Despite the fact that measures of test reliability and validity are available for many medical and psychological tests, this is not the case for most olfactory tests. Indeed, measures of validity (other than a few intercorrelations among different tests) are extremely rare; hence, in this chapter studies of reliability are emphasized (for more discussion on this point, see Schwartz, 1991).

The reliability of a test can be determined in several ways. First, the test can be administered on two occasions to each member of a group of subjects and a correlation coefficient computed between the test scores on the two occasions (termed the test-retest reliability coefficient or the coefficient of stability). Second, when parallel forms of a test are available, the two forms can be administered to the same set of subjects and a correlation coefficient computed between the two forms. Third, subsections of some types of tests (e.g., multiple-item odor identification tests) can be correlated with one another to provide an estimate of test stability. The test is viewed, in this case, as consisting of parallel forms, and the resulting coefficient, when based upon the correlation of half of the items with the other half of the items, is termed the split-half reliability coefficient Since reliability is related to test length, as will be noted below, a statistical correction for test length must be applied to the correlation coefficient obtained in this way to provide the correct reliability coefficient for the full test (Guilford, 1954).

The magnitude of a reliability coefficient depends, to a large degree, on the variation of the test scores of the group upon which it is computed. If all members of a group score exactly the same on a test administered on two test occasions, the reliability coefficient will not be able to be computed, even though, in effect, there is a perfect correlation between the test scores on the two occasions. If only a small variation occurs among the subjects, then the reliability coefficient may be spuriously low. Thus, in assessing reliability one must have some understanding of the variation among the test scores. Also, it should be noted that while a high reliability coefficient indicates that a group of individuals scored similarly relative to one another on a test from one test occasion to the other, all of the individual's test scores still may be lower (or higher) on the second than on the first test occasion. In other words, systematic changes in the test values can occur which are not reflected in the reliability coefficient. In such a case, a high reliability coefficient is misleading, as the overall stability of the test may vary systematically over time.

Although there is a trend among modern developers of olfactory tests to assess the reliability of their instruments, there is a dearth of information on this point in the vast majority of cases. In general, forced-choice odor identification tests with a relatively large number of items evidence a high degree of reliability (e.g., both the test-retest and split-half r's of the 40-item UPSIT are consistently above 0.90) (Doty et al., 1984a, 1985, 1987, 1995). Shorter identification tests evidence lower reliability. For example, the test-retest reliability of the 16-item Scandinavian OdorIdentification Test is 0.79 (Nordin et al., 1998) and that of the 12-item self-administered B-SIT is 0.73 (Doty et al., 1989). Recently, the reliability of the identification component of the 'Sniffin' Sticks' test was reported to be 0.73 (Hummel et al., 1997).

Since it has been reported that olfactory thresholds vary considerably among individuals and evidence considerable day-to-day fluctuations within the same individuals (Stevens et al., 1988), one might expect their reliability to be suspect. Indeed, reliability coefficients for various threshold tests do vary considerable from study to study, and extremely low reliability coefficients have been noted in some cases (e.g., Heywood and Costanzo, 1986; Punter, 1983). Nonetheless, particularly in cases where repeated estimates of the threshold are obtained, respectable reliability coefficients have been reported. Jones (1955), for example, presented ascending concentrations of n-butanol, safrol, and n-butyric acid in sniff bottles (with a comparision blank for

reference) to 24 college students. The series were repeated six times for each subject for each stimulus, and the subjects were required to recognize the substance. Reliability coefficients, based upon intraclass correlations, were 0.82, 0.77, and 0.80, respectively, for the three substances. In a study of 40 subjects, Koelega (1979) reported test-retest reliability coefficients for a four-alternative forced-choice *n*-amyl acetate threshold test to be 0.65, 0.51, and 0.59 for bilateral, right nostril, and left nostril presentations, respectively. In a study of 32 subjects ranging in age from 22 to 59 years, Cain and Gent (1991) reported left nostril:right nostril correlations of 0.68, 0.96, 0.86, and 0.83, respectively, for detection thresholds from single ascending series presentations of butanol, phenyl ethyl methyl ethyl carbinol (PEMEC), isoamyl butyrate, and pyridine. Doty et al. (1995) found test-retest reliability coefficients for detection thresholds of the six odorants contained within the non-forced choice T&T olfactometer test series (skatole, isovaleric acid, γ-undecalactone, β-phenyl ethanol, cyclotene) to range from 0.56 to 0.71; recognition thresholds coefficients were lower, ranging from 0.22 to 0.45. The reliability of the single staircase forced-choice phenyl ethyl alcohol detection threshold was found to be 0.88, whereas the reliability coefficients for single ascending series n-butanol and PEMEC detection thresholds were 0.49 and 0.70, respectively. The reliability of the detection threshold component of the Sniffin' Sticks test has been reported to be 0.61 (Hummel et al., 1997). Doty et al. (1995) concluded that (1) detection threshold values are more reliable than recognition threshold values, (2) thresholds based upon a single series AML procedure are less reliable that thresholds based upon a staircase procedure, (3) reversal location within a staircase series has no influence on reliability, and (4) a clear relationship between reliability and test length (e.g., number of staircase reversals) exists. Importantly, in a related study it was found that the threshold measures tended to load on the same principal component in a principal components analysis as a number of the other test measures evaluated (e.g., the UPSIT, a yes/no odor identification test, and tests of odor discrimination), suggesting that all of these tests measure a common sensory domain (Doty et al., 1994).

V. OTHER CONSIDERATIONS

A. Unilateral Versus Bilateral Testing

Most individuals with chemosensory dysfunction evidence the dysfunction bilaterally (Cain and Rabin, 1989). In cases where unilateral losses are present, they are often unnoticed. When time is at a premium, bilateral testing is preferable to unilateral testing since it reflects clinically meaningful deficits. However, there are a number of occasions when unilateral olfactory testing is of considerable value (e.g., in the detection of some types of tumors) (Doty, 1979), and the ideal assessment of a patient includes unilateral, as well as bilateral, testing.

Unilateral testing is straightforward. Although it is possible to present a stimulus to one naris and obtain mainly unilateral stimulation, the possibility of the crossing of odorant to the contralateral side within the rear of the nasopharynx upon exhalation cannot be excluded. Thus, it is prudent to close the contralateral naris without distorting the septum [e.g., by using a piece of Microfoam™ tape (3M Corporation, Minneapolis,

MN) cut to fit tightly over the borders of the naris] and have the patient exhale through the mouth after inhaling through the nose (Doty et al., 1992). As in the case when both nares are blocked, this precaution decreases the likelihood for air to enter the blocked nasal chamber via the retronasal route.

Furukawa et al. (1988) noted that 7 of 94 patients (7%) they examined, all of whom evidenced no bilateral threshold deficits, evidenced significant unilateral threshold deficits. They reported a similar phenomenon in 6 of 12 patients who had had brain surgery. Of 82 consecutive nonanosmic patients presenting to the University of Pennsylvania Smell and Taste Center with chemosensory dysfunction, 14 (i.e., 17%) were observed whose unilateral detection thresholds were discrepant from one another by at least three orders of magnitude (Doty, unpublished). Interestingly, nine of these 14 individuals were anosmic on one side of the nose, even though only three had bilateral detection threshold values that were obviously abnormal.

B. Detection of Malingering

Because considerable compensation can be available in accident cases for alterations in ability to smell, malingering on chemosensory tasks is not uncommon. It is frequently suggested in the medical literature that if a patient cannot readily perceive the vapors from an irritating substance presented to the nose, he or she is malingering (e.g., Griffith, 1976). However, this is not a definitive method for detecting malingering. Thus, individuals who, on other grounds, are believed to be feigning anosmia usually have difficulty in denying experiencing the effects of NH_3 or other irritants, particularly since these stimuli often produce eye watering, coughing, and other reflexes that are manifested overtly. Furthermore, there appears to be considerable variability among normal individuals in trigeminal responsiveness to such stimulants.

A more valid approach for detecting cheating on the basis of psychophysical testing is to examine response strategies of patients on forced-choice tests, since malingerers often avoid the correct response more often than expected on the basis of chance. This is well illustrated by responses to the UPSIT. Since the UPSIT is a four-alternative forced-choice test, approximately 25% of the test items (i.e., 10) are correctly answered, on average, by an anosmic. The probability of scoring 5 or less on the UPSIT and not having at least some ability to smell is less than 5 in 100. The probability of scoring zero on the UPSIT and having no sense of smell is less than 1 in 100,000.

As noted in Chapter 11, electrophysiological measures are now available that distinguish between intranasal stimulation of the olfactory and trigeminal systems. Although such testing is not possible in all persons, it does allow for a determination as to whether gross responses are present in the olfactory system, adding key information as to the likelihood of malingering.

C. Subject Variables

The reader should be aware that numerous factors influence olfactory function in "normal" individuals and that these factors can significantly alter the ability to smell. Among the variables that meaningfully alter the ability to smell are age, gender, and smoking habits. Of these three factors, age is the most important (for reviews, see Doty,

1991a; Doty and Snow, 1988; Schiffman, 1993). Indeed, over the age of 80 years, nearly three out of four persons exhibit marked olfactory dysfunction; half of those between the ages of 65 and 80 years evidence such dysfunction (Doty et al., 1984b). Age-related declines in olfactory performance are observed for a variety of olfactory tests, including tests of odor detection threshold, identification, discrimination, adaptation, and suprathreshold odor intensity perception (for reviews, see Corso, 1981; Doty, 1990; Murphy, 1986; Schiffman et al., 1979; Weiffenbach, 1984). In addition, age influences the responsiveness of the nasal mucosa to volatile chemicals that produce irritation and other skin sensations (Stevens and Cain, 1986). In general (1) large individual differences are present in the test scores of older individuals, (2) olfactory dysfunction is most evident after the sixth decade of life, and (3) women, on average, evidence age-related declines in odor perception at a later age than do men.

The decline in the ability to smell in later life is not inconsequential. Thus, a disproportionate number of older persons die from accidental gas poisoning (Chalke et al., 1958), and many complain that their food has no flavor (Doty et al. 1984b). The latter phenomenon, which can lead to decreased interest in food, may explain some cases of age-related nutritional deficiencies. As documented clinically (e.g., Deems et al., 1991), decreased "taste" perception during deglutition largely reflects the loss of stimulation of the olfactory receptors via the retronasal route (Burdach and Doty, 1987; Mozell et al., 1969).

In general, women of all ages outperform men on tests of odor identification, detection, discrimination, and suprathreshold intensity and pleasantness perception (Cain, 1982b; Doty, 1986; Doty et al., 1984a; Koelega and Köster, 1974; Le Magnen, 1952). Such differences are present for a wide variety of odorants, including human breath and bodily secretions (Doty et al., 1975, 1978b, 1982), and are observed as early as such testing can be reliably performed (Doty, 1986). The fact that female babies more readily show a preference for odors from their own mothers than do male babies suggests that such sex differences are present at birth and are either inborn or due to early developmental sexually dimorphic influences (Makin and Porter, 1989) (see Chapter 15).

The influence of tobacco smoking on olfactory function is less marked, on average, than that of age or gender (e.g., Doty et al., 1984b). This influence, however, is doserelated and present in both previous and past smokers (Frye et al., 1990). Interestingly, cessation from smoking results in some improvement of olfactory function over time—improvement that is related to the amount of previous smoking and the duration of such cessation.

Both reversible and irreversible changes in smell function have been observed following exposure to a wide variety of environmental agents, including industrial chemicals and dusts (see Chapter 27). In the most extensive study on this point, the olfactory function of 731 workers at a chemical plant that manufactures acrylates and methacrylates was tested (Schwartz et al., 1989). Decrements in odor identification test scores proportionate to the estimated dose exposure levels of these acrylates were found. Interestingly, individuals who had never smoked cigarettes but who had been exposed to acrylates were six times more likely than their nonexposed counterparts to evidence olfactory decrements.

Prior experience with odors, particularly that obtained on taste and smell organoleptic panels, clearly influences measures of the ability to smell. For example, repeated testing

within the perithreshold odorant concentration range results in decreased thresholds or enhancement of signal detection sensitivity measures (Doty et al., 1981; Engen, 1960; Rabin and Cain, 1986; Wysocki et al., 1989); practice with feedback influences the ability to name odors (Desor and Beauchamp, 1974; Engen and Ross, 1973). Interestingly, the hedonic quality of odorants can be influenced by repeated exposure, making unpleasant odors less unpleasant and pleasant odors less pleasant (Cain and Johnson, 1978). Assuming that adaptation is not the primary basis for this phenomenon, affective components of odors appear to habituate somewhat independently of odor intensity.

D. Adaptation

Exposure to an odorant, if recent and relatively continuous, can produce a temporary decrease in its ability to be perceived, empirically reflected, for example, by heightened detection threshold values or decreased intensity ratings (for a review, see Cometto-Muñiz and Cain, 1995). Some chemicals produce a decrement in the perception of other chemicals (termed cross-adaptation). Fortunately, most modern clinical olfactory tests are either little influenced by adaptation or operationally are standardized in such a way that any adaptation that occurs is unlikely to meaningfully influence the test results. For example, the UPSIT was designed to minimize adaptation by (1) employing largely multicomponent "natural" odorants, (2) requiring minimal sampling of each odorant, (3) having verbal, rather than odorous, response alternatives, (4) ordering the presentation of odorants such that dissimilar odorants follow one another (thereby minimizing cross-adaptation), and (5) allowing adequate time between the smelling of each odorant item (Doty et al., 1984a).

Several general rules have emerged from studies of adaptation that are worthy of note (Cometto-Muñiz and Cain, 1995; Köster and De Wijk, 1991; Stuiver, 1958). First, the amount of adaptation induced is a function of the duration of exposure and the concentration of the adapting stimulus. Second, the subject's attention level influences the degree of adaptation. Third, the rate and degree of recovery from adaptation are a function of the magnitude and duration of the adapting stimulus. Fourth, cross-adaptation is most commonly asymmetrical. For example, while exposure to odorant A decreases the perceived intensity of odorant B, exposure to odorant B may not decrease the exposure to odorant A to the same degree. Fifth, the sensitivity to a given odorant is typically reduced more by the exposure to that odorant than to any other odorant. Sixth, in rare instances an odorant may have a larger adapting effect on the sensitivity to another odorant than it does on itself. Seventh, the sensitivity to an odorant that self-adapts strongly is usually also reduced strongly by other odorants. Eighth, adaptation of one side of the nose produces adaptation, albeit less, in the other side of the nose. Ninth, adaptation to complex odorants (i.e., odorants made up of more than one chemical) is generally less than adaptation to single-component odorants. Finally, adaptation to odorants can be relatively rapid. For example, Aronsohn (1886) found that subjects continuously exposed to the vapors of lemon or orange oil reported complete loss of olfactory sensations, on average, in 3 minutes (range: 2.5–11 min). Recovery occurred in about the same time required to induce the loss.

VI. THE PERCEPTION OF ODORANT MIXTURES

As noted above, a number of modern olfactory tests, including the UPSIT, employ stimuli that, for the most part, are complex mixtures of chemicals, mimicking stimuli encountered in everyday life. More often than not such stimuli are perceived as a unitary gestalt and given a name associated with the object or source from which they are known to emanate—cinnamon, pizza, cheese, gasoline, orange, lemon, walnut, etc. (see Livermore and Laing, 1998b). There is considerable clinical utility in using such tests, since many receptor types are activated. This is in contrast to threshold tests employing single odorants, as they presumably examine the responses of the olfactory system to a smaller subset of receptors. It has been shown that rodents who have sustained damage to 80–90% of their olfactory receptor cells still retain their ability to detect some single odorants. Similarly, odor sensitivity is retained unchanged when large lesions have been made in the bulb. Therefore, from at least a theoretical standpoint, major changes in the olfactory system can occur and not be detectable by the use of some single odorants. In contrast, the perception of mixtures invariably involves inhibitory interactions at the bulb (and possibly other olfactory centers) that occur through complex neural circuitry. Lesions that disrupt the circuitry are likely to alter the characteristic suppression effects observed between odors in mixtures. Rat data indicate that lesions involving much of the bulb can result in the failure to re-learn a mixture analysis task, compared to their successful retention of odor sensitivity and ability to discriminate between odor qualities (Slotnick et al., 1997).

How is it that mixtures of chemicals end up providing a largely unitary perceptual gestalt? How much information, in terms of discriminating individual components, can humans obtain from complex mixtures? If one odorant suppresses the odor of another (as is seen in the case of deodorants or room fresheners), how does this relate to the relative concentrations of the odorants within the mixture? Are there psychophysical rules or laws explaining mixture relationships? These and other questions related to odorant mixtures are the basis of the remainder of the chapter.

A. Effects of Mixing Odorants on Their Perceived Intensity

Usually when two single compound odorants are mixed together, the perceived intensity of one or both is altered substantially, the net result being a lowering of the intensity of the components. However, on rare occasions enhancement may occur. In early mixture studies, Aronsohn (1886) reported that the odor of camphor was neutralized by such odors as gasoline, cologne water, and oil of juniper, and Nagel (1897) found that counteraction between two odorants could result in both being rendered almost odorless. Zwaardemaker (1900), the most famous of early olfactory scientists, confirmed these observations for a number of mixtures using an olfactometer and demonstrated that the extent of perceptual interactions between two odorants was more dependent on their concentrations than on their qualities. Similar results have been reported by others, including Moncrieff (1959) and Jones and Woskow (1964), the latter reporting that the perceived intensity of a binary mixture, although less than the sum of its component intensities, is more than a simple average of the two.

Zwaardemaker (1930) conceptualized the mutual weakening of the perceived intensity of a mixture of two components as follows: "The two sensations can be imagined as two vectors representing two forces counteracting each other in our intellect." The interaction between two odorants was later formalized by Berglund et al. (1973) in a mathematical model that incorporated the application of vector addition to odor mixtures for the prediction of the overall intensity of mixtures. Although the vector model has received widespread attention (e.g., Berglund, 1974; Berglund and Olsson 1993a; Berglund et al., 1976; Cain, 1975; Cain and Drexler, 1974; Moskowitz and Barbe, 1977; Laing et al. 1984; Olsson, 1994), after two decades of investigation its best predictions have been for simple binary mixtures. Other models for predicting the perceived intensity of simple mixtures have been proposed (e.g., the Strongest Component Model, the U Model, and the UPL Model; see Laffort and Dravnieks, 1982). Such models are modifications of the vector model, but have not been extended to multicomponent mixtures. The most recent model in this series was the UPL2 model (Laffort et al., 1989) which incorporated the power function that normally relates perceived odor intensity to concentration. The ERM model of Schiet and Frijters (1988) was also based on a power function relating these factors and, although applied with some success to simple gustatory mixtures, was not an improvement in the models just described for olfactory mixtures. As summarized by Cain et al. (1995), "the principle by which psychophysical information on single components reflects itself in a model of interaction seems to evade the psychophysical models presented here" (all the above).

Clearly, none of the aforementioned models adequately describe the changes in perceived intensity for all pairs of odorants examined, and none have been demonstrated to reliably predict the intensity of mixtures containing more than two odorants. Booth (1995) provides an interesting critique on the modeling of odor interactions but provides no firm ground for future studies to proceed. Among a number of shortcomings, none of the above models have been based upon the receptive and neural processes that underlie the perception of mixtures, nor has attention been given to choosing odors that have physicochemical features that might provide some basis for antagonistic interactions. Furthermore, these models have provided no insight as to the nature of the sensory processes, and none adequately predicts the intensity of multicomponent mixtures. Present evidence suggests that addition or partial addition of the perceived intensities of the components of mixtures occurs with binary and ternary mixtures; beyond this number of components neural processes limit intensity addition (Berglund et al., 1976; Laing et al., 1994a; Moskowitz and Barbe, 1977).

The interactions noted above concern suprathreshold concentrations of odorants and provide examples of where the sense of smell compresses rather than adds intensity information. In contrast, additivity of neural input appears to be inherent in mixtures containing only sub-threshold quantities of odorants (Laska and Hudson, 1991; Laska et al., 1990). Indeed, in mixtures with only three odorants, the magnitude of the addition was noted by Laska et al. to be substantial and to often exceed that obtained from simple summation. Patterson et al. (1993) reported instances of near-true additivity of subthreshold components and suggested that additivity may function to enhance sensitivity to the typically complex (and often subthreshold) odor stimuli encountered in everyday life. They noted that the number of chemicals activating the system could be as

important as the strength of any one of the odorants, providing a type of "biological economy" of the input.

B. Discrimination of Components in Odorant Mixtures

Since, as mentioned earlier, odors are commonly encountered as mixtures in our environment, an important characteristic of the human sense of smell is to discriminate differences between mixtures. Discriminating the odors of fresh and "off" milk, ripe and overripe fruit, cork taint in wine, and various perfumes are examples. In the area of pollution control, changes in the complex odor of sewage provide engineers with an insight as to the part of the treatment process that is not functioning properly; sulfides emanate if the anaerobic process is malfunctioning, and sour, rancid, and acid odors appear if the sludge treatment is inappropriate. In studies with binary mixtures, Rabin (1988) and Rabin and Cain (1989) showed that humans are particularly sensitive to the presence of small amounts of odorants that are not normally found in a stimulus. They reported that (1) high familiarity with a major component and the ability to label it consistently facilitates the detection of a minor component, (2) the minor component is not detected as readily if it is unfamiliar, and (3) unpleasant stimuli are more detectable than pleasant ones, although the effect was not as large as the effect of familiarity. Experience, therefore, and to a lesser extent pleasantness, improves discrimination between two single odorants or two mixtures, suggesting that similar cognitive processes operate with the two types of stimuli.

Although the Rabin studies suggested that humans are very sensitive to small changes in an olfactory stimulus, Laska and Hudson (1992) reported that relatively large changes in the composition of mixtures are sometimes required for discrimination to occur. Thus, discrimination of 3-, 6-, or 12-component mixtures from the same mixtures minus 1 component produced error levels of 20–40%, with the level depending on the type of odorant that was removed. Accordingly, the dependence on the type of odor removed precluded defining a limit in the ability of humans to discriminate between two complex mixtures.

C. Identification of Components in Odorant Mixtures

Prior to studies of the abilities of humans to analyze mixtures, informal information from perfumers and flavorists suggested that between 5 and 30 components may be identified in mixtures (D.G.Laing, unpublished data). Over the past decade it has become clear that these numbers are an overestimate, as most individuals, including perfumers, are only able to identify up to 3 or, rarely, 4 components. An early hint that only a small number of odorants can be identified in mixtures was apparent in the report by Berglund (1974), who suggested from studies of the addition of the perceived intensities of components, that an analytic or additive process occurred up to 3 components, whereupon above this number an interactive process predominated. The latter was apparent as an asymptote in the total perceived intensity of a mixture, with little change occurring as the number of components increased. In accord with this notion, Moskowitz and Barbe (1977) found that in some instances the overall intensity of 5 component mixtures was less than that of mixtures with fewer components.

In perhaps the first formal scientific studies on this topic, Laing and Francis (1989) and Livermore and Laing (1996) reported that training and experience did not increase the number of components identified with subjects that had been trained for a few minutes, 3 weeks, or who were perfumers and flavorists, the maximum still being 3–4. Varying the task or the odorants resulted in no improvement in the number identified; thus, in another study a selective attention procedure was not more efficient than a procedure that required subjects to identify as many components as possible during an ad lib sampling method (Laing and Glemarec, 1992). Futhermore, this maxima was not altered if the odorants used were those classified by perfumers as "poor blenders," i.e., odorants that they used to "stand out" in mixtures (Livermore and Laing, 1998a). Schiet and Frijters (1988), using another approach to this problem, reported that subjects invariably underestimate the number of components in mixtures containing up to 4 components. A similar result was obtained by Jellinek and Köster (1979), whose subjects found the odor of single chemicals to be as complex as that of mixtures.

Clearly, the data of the aforementioned studies indicate that there is a significant limitation in the olfactory system in the processing of information from more than about 3 odorants. Mixtures of complex odors tend to behave like mixtures of single odorants, with a maximum of about 3 being identified in stimuli containing up to 8 complex odors. The possibility that the entry of hundreds, perhaps thousands, of odorants into the nose would produce a nonidentifiable smell sensation has not yet eventuated (Livermore and Laing, 1998b).

D. Mechanisms Involved in Odor Mixture Perception

The limited ability of humans to discriminate and identify odorants in mixtures is likely due to a number of mechanisms. Changes in spatial processing arising from competition for receptor sites and cells at the periphery, and inhibition in the bulb and at other olfactory centers, would be expected to reduce the information within the activated receptor cell arrays, making it difficult to recognize the patterns of activation due to different odorants. Since temporal processing favors the first processed odorant, the initial odorant has the opportunity to act as an antagonist towards other odorants at the periphery and to inhibit neural activity arising from other odorants in the bulb. However, if the delivery of different odorants in ternary or more complex mixtures to the nose is less than the time for processing two odorants in working memory, the latter becomes the ultimate limiting factor as regards the number of odorants identified. These mechanisms are discussed in detail below.

1. Spatial Processing

As noted at the beginning of this chapter and elsewhere in this volume, a given odorant activates unique arrays of receptor cells in the nose (Kauer, 1991; Mackay-Sim et al., 1982), which, in turn, are reflected by patterns of activation of glomeruli and mitral/tufted cells in the olfactory bulb. Different odors produce different arrays that represent the spatial codes of identification. However, when a mixture of two odorants is sensed and the perception of one or both is suppressed to some degree, the arrays representing the two stimuli in the bulb show a reduction in the number of glomeruli that are activated

(Bell et al., 1987; Joerges et al., 1997). If the suppression of one of the odorants is such that it cannot be perceived, little of the normal array of activated glomeruli is seen (Bell et al., 1987). The suppression may be due to fewer receptor cells being activated (Ache et al., 1988; Kurahashi et al., 1994; Simon and Derby, 1995) because of competition by the odorants for the same receptor sites, resulting in less input to the bulb. Suppression can also be caused by lateral inhibition between glomeruli or mitral cells in the bulb (Pinching and Powell, 1971; Shepherd and Greer, 1990; White, 1979). The loss of identity of up to 5 odorants in 8-component mixtures (Livermore and Laing, 1998a) prompted Jinks and Laing (1999) to propose that the competition and inhibition between odorants could result in no odorant being identified in mixtures containing double this number of components. Their psychophysical study showed that 1 and zero components were identified in 12- and 15-component stimuli, respectively. The fact that the 15-component stimulus had an odor, albeit not one that could be associated with any of the components or an object or source, indicates that neural input from some or all of the arrays characterizing the components was registered.

In light of such observations, it is interesting to note that, in the rat, neural images of complex olfactory stimuli, including rat nest odors comprised of volatiles from urine, feces, and bodies (Stewart et al. 1979), have shown that the number of activated glomeruli is similar to that found with a simple single odorant such as limonene (Bell et al., 1987). Therefore, spatial processing of single and complex odorants involves both peripheral and bulbar interactions that reduce and simplify identification. Accordingly, the olfactory system uses spatial coding to analyze and identify single odorants when presented alone and in simple mixtures and simplifies identification of complex mixtures by combining the remaining parts of the arrays into a single characteristic array that is associated with the object or source of the stimulus. This interpretation is in agreement with the finding of Jellinek and Köster (1979) that single odors are perceived to be as complex as those of mixtures.

But there is another aspect to spatial processing. An intriguing feature of single odorants and odor mixtures is that they can be characterized by several qualities or "notes" (Laing and Willcox, 1983; Moskowitz and Barbe, 1977). Hexenal, for example, is described as having "green" and "fatty" qualities, and ethyl butyrate as "sweet" and "fruity." However, when single odorants are components of mixtures but cannot be identified, often one or more of their qualities can be discerned. Recently, Jinks and Laing (2001) investigated the qualities of binary, ternary, and quaternary mixtures of four dissimilar odorants to determine the information about odor quality that needs to be retained for identification of the odorant. The data indicated that failure to identify an odorant could occur with loss of some but not all of the qualities. However, failure could also occur when the major qualities were present but the ratios of their perceived intensities were substantially altered. This suggested that a different smell could be produced using the same qualities but in different ratios. Identification, therefore, was affected by the type and/or the perceived intensity of the qualities of an odorant. These results were interpreted in terms of a Configurational Hypothesis of Olfaction, in analogy with the Configurational Hypothesis of Facial Recognition (Enns and Shore, 1997; Rakover and Teucher, 1997). In brief, in the case of a face, identification of a person not only requires certain features to be present in a drawing or photograph, but these features must be in the correct proportion to each other. Similarly, identification of an odorant or a

complex mixture requires some of the characteristic qualities in the correct proportions to be perceived.

But what is the neural basis of a quality or "odor note," and how is it represented in the spatial code? Thanks to advances in molecular biological studies of the chemoreceptive process, an insight into this problem is possible. For example, as noted at the beginning of this chapter, it is commonly accepted that each human receptor cell has only one type of receptor (Rawson et al., 1997) and that there are ~1000 receptor types, as indicated by the number of receptor genes (Buck and Axel, 1991). Stimulation of receptor cells by a single odorant will result in a variety of cells being activated in accordance with the degree or "ease of fit" of the odorant to each receptor site type. If the fit is predominantly to two or three receptor types, they will be the main inputs to the array of glomeruli and mitral/tufted cells activated in the bulb. However, the conformations adopted by an odorant to fit the two to three receptor types will be dictated by the structural features of the odorant and receptor molecule. In one conformation a molecule may be aligned within a receptor site according to its length and functional group, e.g., the 17 receptor for octanal (Araneda et al., 2000); in another it may sense a structural feature common to a number of odorants, e.g., an 8-carbon chain containing a terminal carbonyl group common to aliphatic aldehydes, acids, esters, and ketones (Imamura et al., 1992). Since the overall odors of these latter aliphatic carbonyl substances are easily discriminable (Laska et al., 2000), each odorant must require at least two receptor types to be occupied for this to occur. Accordingly, it is tempting to suggest that activation of the cells with the common receptor for these odorants results in an odor quality common to each odorant, while activation of the cells unique to each odorant produces a quality unique to each odorant. In addition, the spatial map of each odorant should show glomeruli or mitral/tufted cells that are activated by all four odorants and others that only one of the odorants will activate. From the limited data available, it is suggested that the conformations an odorant can adopt in different types of receptors defines the important structural features that provide the qualities perceived. This interpretation suggests that the spatial code for an odorant contains information about molecular structure and odor qualities. In contrast, the spatial map of complex mixtures such as chocolate aroma, where none of dozens of odorants can be identified, will be composed of input from receptor cells representing features of many odorants, and it may be the location and magnitude of the input to the bulb rather than molecular features that define its identity. Nevertheless, several qualities can usually be discerned in complex aromas, and these are likely to be those that remain from individual odorants in the mixture which are insufficient to identify the latter but contribute to the overall aroma of the complex mixture.

2. Temporal Processing

During the 1980s, Getchell et al. (1984) reported that odorants can differ by hundreds of milliseconds in the times they take to activate receptor cells, while Kuznicki and Turner (1986) showed that humans require different reaction times to recognize the four common tastants. These findings prompted Laing (1987) to propose that if the time differences between the activating times of odorants at the periphery were maintained as the neural message traveled through the bulb and other olfactory processing centers in the

brain that dealt with memory and identification, then a "fast" odorant would have a number of advantages if presented in a mixture with a "slow" odorant. For example, the faster odorant may be more successful in competition for receptor sites and cells, and being the first to activate the bulb, it could trigger lateral inhibition between glomeruli or between mitral cells to further reduce neural input from the slower odorant. Accordingly, it was predicted that the faster odorant would be the first odorant identified in a mixture, the slower odorant would incur the greatest suppression of intensity, and the number of cells and glomeruli in spatial arrays activated by the latter odorant would be reduced.

To investigate the first two of the above predictions, Laing et al. (1994b) used a specially designed computercontrolled olfactometer, which allowed odorants to be delivered together in a mixture or in series separated by intervals as small as 50 ms. By asking subjects which of two odorants was perceived first during a trial and varying the time between delivery of both odorants from 100 to 600 ms, the processing time difference between them was established as that which produced a chance response, i.e., 50% for the forced-choice yes/no task. The magnitude of the differences varied from zero to more than a second and was dependent on both the quality and perceived intensity of the odorants, with the latter being more important. Perceived intensity was also reduced more for the slower odorant. With both predictions upheld, the existence of temporal processing and its implications for mixture perception were demonstrated. A later study (Jinks and Laing, 1999b) confirmed that knowledge of processing time differences allowed predictions of which odor would be perceived first in other mixtures. Thus, they showed that when odor A was perceived before B and B was perceived before C, that A was perceived before C, demonstrating that transitivity had occurred (Fig. 7). However, investigation of temporal processing in ternary mixtures revealed a substantial limitation in the ability of humans to indicate which odor is perceived first and the existence of a third mechanism that affects perception of components in odor mixtures (Jinks and Laing, 1999b). Temporal processing of ternary mixtures and the third mechanism, which is postulated to involve olfactory working memory, are discussed below.

3. The Role of Memory

The perception of the order of processing odorants in ternary mixtures, however, has proved to be very difficult (Jinks and Laing, 1999b). Initial experiments indicated that subjects recorded chance level responses when asked to indicate which odorant was perceived first or last. To investigate whether the chance results were due to a limitation in the capacity of olfactory working memory to process both order and identity of the odorants, presentation of the third odorant was delayed by 300, 600, and 900 ms. With one of the two sets of three odorants studied, the results indicated that a delay of between 600 and 900 ms was needed before the usually faster odorant was perceived first (Fig. 8). With the other set, subjects recorded chance responses even with the 900 ms delay. The mean responses of subjects, when asked to identify the odorants in the mixture or delay conditions, showed that this was at chance level. The result is in agreement with the earlier studies of Laing and colleagues, who found that few subjects could identify all the components of ternary mixtures. Overall, the results with ternary mixtures indicated that a mechanism related to the speed of information retrieval about the identity or temporal order of the components was the cause. The most likely candidate appears to be the

inability of olfactory working memory to process the information about the identity and order of the first two components before neural input from the third began to be processed. Although it is not fully understood, working memory is defined as the "system

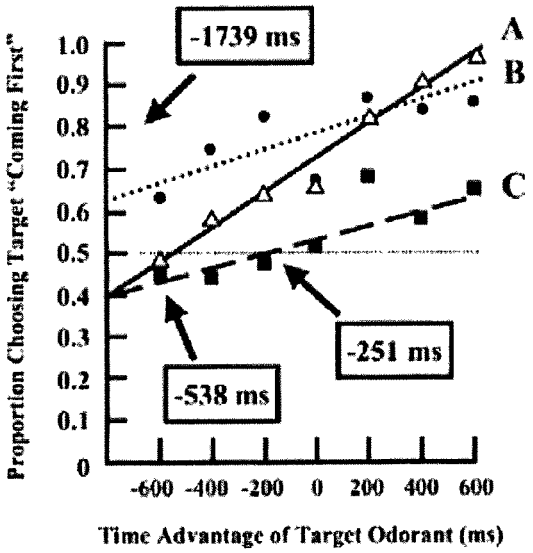

Figure 7 Regression lines representing the proportion of trials an odor in a binary mixture was perceived "first" when presented with a time advantage, disadvantage, or as true mixture (0 ms interval). Arrows and times in boxes indicate when both odorants were perceived first on 50% of trials. (A) Stimulus of coniferan and triethylamine with coniferan being perceived 538 ms before triethylamine; (B) a stimulus of carvone/triethylamine with carvone perceived first 1739 ms before triethylamine; (C) a stimulus of carvone/coniferan with carvone perceived first 251 ms before coniferan.

responsible for the temporary storage and manipulation of information, forming an important link between perception and controlled action" (Baddeley, 1998). The process

of identifying an odor within working memory is likely to involve several steps: encoding of the odor by neurons, recalling of the

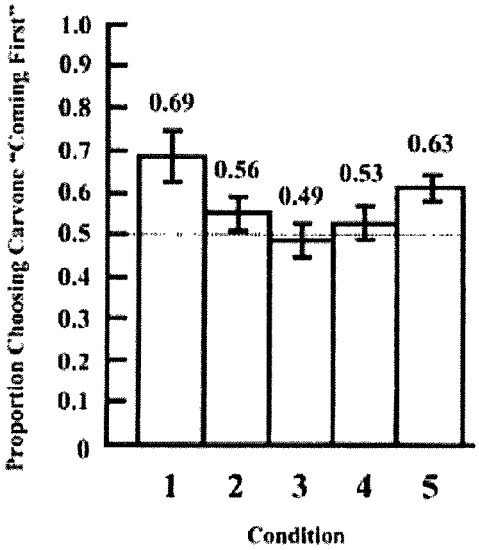

Figure 8 Proportion of trials (numbers above bars) in which subjects selected an odor "coming first" in binary and ternary mixtures and mixtures where the presentation of triethylamine was delayed. Conditions: 1, binary mixture of carvone/coniferan; 2, ternary mixture of carvone/coniferan/triethylamine; 3, 4, and 5, ternary mixture with the presentation of triethylamine delayed by 300,600, and 900 ms, respectively. Open and shaded bars indicate that the means were significantly/not significantly different from 0.5 (chance), respectively.

coded representation of the odor from long term memory, comparison of the two representations, and the judging and responding to the representations. This type of process has been proposed for visual information (Eskandar et al., 1992). Indeed, the interference of a third odorant with the perception of others is reminiscent of that reported

for visual spatial memory, where it was proposed that an irrelevant visual stimulus may have obligatory access to a visual store and interfere with the storage and processing of other visual spatial information in working memory (Toms et al., 1994). Limitations in the capacity of olfactory working memory to process more than two odorants within 600–900 ms appears to be a major factor limiting the discrimination and identification of odorants in multicomponent mixtures. Such a finding has implications for the perception of odorants released during an eating episode where many can be released within the processing time differences cited here, but only a few may be identified. Controlled release of odorants from different food media could, however, allow products to be developed with high flavor impact.

VII. CONCLUSIONS

The present chapter has provided an up-to-date review of the psychophysical means for testing the human sense of smell and has examined how the human olfactory system likely integrates information from complex arrays of odorant chemicals which, individually, would seem to produce conflicting odorous sensations. It is of interest that relatively high correlations exist among the scores derived from nominally distinct olfactory tests, regardless of whether they are based upon single- or multicomponent stimuli. Test reliability has been shown to be largely a result of test length, irrespective of the nature of the stimuli included in the tests. To what extent tests employing multicomponent odors are superior to ones employing single odorants is an empirical issue, although it would seem that by sampling more elements of the system, a test should be more sensitive. Continued efforts to refine the procedural elements of olfactory tests should help in the development of test batteries sensitive to wider ranges of olfactory deficits than those that are currently available.

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